Remarks/Arguments

Claims 67 to 78 remain in the application. The subject matter of claims 68 to 72 is restricted by the amendments above, to the elected invention of treating tumor related disorders. This was done by replacing claim 68 with new claim 78 which is dependent on claim 73. That is, these claims are restricted to cachexia which is a tumor related cachexia.

The present invention is rejected under 35 U.S.C. 103(a) as being *prima facie* obvious over Kimura et al. (EP 0799823) and Ruff et al. (J. of Clin. Invest. Vol 73).

Applicants respectfully submit that it is not obvious to combine those two references to reject the present invention because of differences between tumor relate cachexia and the non-tumor related cachexia described in the cited art.

As noted above, the claims are restricted to the treatment of "cachexia" that is a tumor related disorder" and that "cachexia caused by sepsis" is not covered by the scope of the claims.

The difference between cachexia in cancer and that in sepsis, is significant with regard to causes of cachexia. The

art provides evidence that the main factor to cause cachexia in cancer (tumor) is different from that in sepsis. For example, Tumor Necrosis Factor-α is reported as such a main factor in sepsis (see Infect. Immun. 1999 67, 1079-1085 and Nature Vol. 330 17 December 1987, 662-664 - copy annexed), while Leukemia Inhibitory Factor and Interleukin-6 are a factor in cancer (see Biochem. Biophys. Res. Commun. 1989 May 15, 160(3), 1085-1092 and Cytokines Mol. Ther. 1995 Jun. 1(2), 107-13, Review - copy enclosed). There is no reason of record to conclude that teaching with respect to one type of cachexia is obviously applied to another type, having a different genesis. Applicants therefore submit that it is not obvious to a worker in the art that the two cachexia, that is, cachexia in cancer and in sepsis, should be dealt with in the same way. More specifically, it is not obvious that a skilled person would conclude that a drug effective against septic cachexia would also be effective against cancer cachexia with a reasonable expectation of success. At best it might be a consideration to try, but there is no basis to conclude that one would be successful.

In addition, even if Ruff et al. were applicable, applicants submit that Ruff et al. does not support the conclusion that

there is a relationship between muscle wasting and prostaglandin in cachexia, which arises from sepsis. Ruff et al. does not provide sufficient teaching to support a conclusion of such a relationship for the following reasons.

Ruff et al. reports that indomethacin, one of prostaglandin synthesis inhibitors, inhibited muscle wasting, but does not provide any data on prostaglandin in muscle during the experiment. Therefore, the experiment using indomethacin incompletely supports the relationship between prostaglandin and muscle wasting because of lack of data on prostaglandin itself. In addition to indomethacin, acetaminophen is also tested by Ruff et al, and they present data showing that acetaminophen did not suppress muscle wasting. It is noted that acetaminophen was known to lower prostaglandin in gastric and duodenal mucosa (see Gut. 1981 Apr, 22(4), 283-9, paracetamol is another name of acetaminophen) and, therefore, was thought to inhibit the prostaglandin synthesis at peripheral tissues. If the inhibition of prostaglandin synthesis was responsible for the inhibition of muscle wasting as the Examiner concludes, acetaminophen should have inhibited muscle wasting as well as indomethacin, but it does not in Ruff et al. Therefore, the experiment using

acetaminophen should prevent a person skilled in the art from concluding that the inhibition of prostaglandin synthesis results in the inhibition of muscle wasting.

For the reasons mentioned above, the applicants believe that the Examiner erred in premising the relationship between prostaglandin synthesis and muscle wasting in septic cachexia on the teaching in Ruff et al. Furthermore, even if such a relationship were shown by Ruff et al. there is no support in the art to conclude that it is obvious to combine Kimura et al. with Ruff et al. and apply the resulting teaching because they are concerned with a different type of cachexia having a different cause.

In view of the above, it is submitted that the present invention is not shown or suggested by the cited art. Withdrawal

of the rejections and allowance of the application are

respectfully requested.

Respectfully submitted,

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Encs. BREUILLE, et al., "A Sustained Rat Model for Studying the Long-Lasting Catabolic State of Sepsis"; Infection and Immunity, Mar. 1999, pp. 1079-1085, Vol. 67, No. 3

TRACEY,et al., "Anti-cachectin/TNF monoclonal antibodies prevent septic shock during lethal bacteraemia", Nature, pp.662-664, vol. 330

MORI et al, "Purification of a Lipoprotein Lipase-Inhibiting Protein Produced by a Melanoma Cell Line Associated With Cancer Cachexia", Biochemical and Biophysical Research Communications, May 15, 1989, pp. 1085-1092, Vol. 160, No. 3

STRASSMANN et al., "Inhibition of experimental cancer cachexia by anti-cytokine and anti-cytokine-receptor therapy", Cytokines and Molecular Therapy, 1995, pp. 107-113, vol. 1

KONTUREK, et al., "Distribution of prostaglandins in gastric and duodenal mucosa of healthy subjects and duodenal ulcer patients: effects of aspirin an paracetamol", Gut, 1981, pp. 283-289, vol. 22